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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,893	07/08/2005	Christopher Gregory	21099.0076U2	9625

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EXAMINER	
WARE, DEBORAH K	

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,893	GREGORY ET AL.	
	Examiner	Art Unit	
	DEBBIE K. WARE	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 7-10* is/are pending in the application.

4a) Of the above claim(s) *7-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3 and 7-10 are pending.

Response to Amendment

The amendment filed February 17, 2009, has been received and entered. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Further, Applicants comment regarding the restriction is noted and to correct the record, the previous sentence was a grammatical typo wherein the term "not" was placed in the wrong place in the sentence and should have been placed after "there is" which occurs in line 3, of page 2, under the heading "Election/Restrictions" of the last Office action. Hence, with this correction at line 3, noted above, would read "inventions are independent or distinct and there is not a burden upon the Examiner" as argued by Applicants in their rebuttal to the restriction requirement in the last response submitted by Applicants.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on July 29, 2005, was filed and received on July 29, 2005. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-3, in the reply filed on November 9, 2007, is acknowledged. The traversal is on the ground(s) that the claimed inventions are not independent or distinct and there is a burden upon the Examiner. This is not found persuasive because the kit of Group III does not require the method steps of Group I, and the method does not require the kit. The kit requires separate elements not required of Group I and a reference which read on Group I will not necessarily read on Group II. For example, Group II requires biliverdin and Group I, requires samples of avian or reptilian species. There are different technical features required of each Group I and II, and the restriction is deemed proper.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 lacks antecedent basis for the recitation of "the absorbance value" at line 4. Claims 2-3 lack antecedent basis for the recitation of "a change" at line 4. Also claims 2-3 are rendered vague and indefinite because it is unclear what an "increased biliverdin concentration" and "an above-normal biliverdin concentration" as recited,

respectively, are intended to encompass in terms of the actual concentrations in the sample. The metes and bounds of the claims can not be determined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yein et al (US 5783407) in view of Falchuk (US 6902881), Lin et al (US 5284940) and DERWENT (AC No: 1987-173702).

Claims are drawn to methods of determining/measuring biliverdin in a sample from avian or reptilian species comprising contacting the sample with biliverdin reductase, measuring change in absorbance at about 325 to about 750 nm and

comparing with absorbance values from a control sample or a standard concentration curve.

Yein et al teach a method of determining/measuring biliverdin (col. 2, lines 20-21) concentration in a sample comprising contacting the sample (col. 2, line 24, e.g. tissue) with an oxidizing enzyme (col. 2 , lines 60-64), measuring a change in absorbance within a range of 325 to about 750 nm (col. 6, lines 15-21, lines 27-30, lines 51-53) and determining/measuring biliverdin concentration by comparing the absorbance values to a control or a standard curve (col. 7, lines 51-52 and lines 7.

Falchuk teaches samples which comprise biliverdin, see col. 12, lines 36-41 and line 66. The sample is from an avian or reptilian species, note col. 27, line 4.

Lin et al teach that biliverdin may be converted to bilirubin by the enzyme bilverdin reductase. Note col. 14, lines 58-60.

DERWENT teaches that reductase enzyme is an oxidizing enzyme. See abstract, line 2.

The claims differ from Yein et al in that a sample from an avian or reptile species, and biliverdin reductase is not disclosed.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to select a sample which comprises biliverdin from snakes or birds and further to add the enzyme, bilverdin reductase, in an assay disclosed by Yein et al because biliverdin is clearly disclosed to be in snake and bird species by Falchuk and Lin et clearly teach bilverdin reductase and DERWENT teaches that reductases are oxidizing enzymes.

Thus, one of ordinary skill in the art would have expected successful results for determining biliverdin concentration in a bird or snake sample using an enzyme reaction mixture of the sample and biliverdin reductase since the enzyme is well recognized to be an oxidizing enzyme and can convert biliverdin to bilirubin and oxidizing enzymes can also convert bilirubin to biliverdin.

Hence, the determination/measurement of biliverdin would have been an expected successful result by such enzyme reaction mixture and to measure a change in absorbance between 325 to about 750 nm is clearly disclosed by Yein et al as noted above, or is at least suggested by Yein et al. Also, Yein et al clearly recognize that each of biliverdin and bilirubin can be determined or measured based on absorbance values taken and compared with absorbance values on a standard curve or from a control sample.

The claimed process steps are well recognized by the cited prior art and one of skill would have been motivated to provide for these steps to determine and/or measure biliverdin concentration in a sample from an avian or reptilian species. The absorbance range is clearly suggested, if not taught, by the cited prior art and an increased biliverdin concentration in the sample is suggested. Since just as the enzyme reaction of bilirubin oxidase can be used to measure bilirubin by oxdizing bilirubin to biliverdin, the enzyme reaction of biliverdin reductase can be used to measure biliverdin by the conversion of biliverdin to bilirubin.

The claims are taught, or are at least suggested, and there is sufficient motivation demonstrated by the cited prior art to carry out the process steps as claimed

to determine biliverdin concentration in a sample from birds or snakes. The claims are, therefore, rendered prima facie obvious over the cited prior art.

Response to Arguments

Applicant's arguments filed February 17, 2009, have been fully considered but they are not persuasive. The argument that Yein et al disclose solely biliverdin as the product and not as the object for detection is noted, however, this is incorrect because Yein et al disclose the product can be detected, see last two lines of the abstract, for example. Also, Applicants' point that the patient is human is noted, but this is not necessarily true in point because animals can be patients too. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The argument that Yein et al has no disclosure regarding a reducing enzyme is noted, however, Lin et al, which has been applied as a secondary reference teach that biliverdin may be converted by the enzyme bilverdin reductase. Different product species concentrations can be detected by measuring a change in their absorbance using a spectrophotometer, and this is well known by one of ordinary skill in the art. Also depending upon the desired product species, selection of an appropriate enzyme for converting from one product species to another, especially with reactants such as biliverdin or bilrubin is clearly within the purview of an ordinary artisan.

Also, the argument that birds or reptiles are not suggested by Yein et al is noted, however, Falchuk teach that samples of biliverdin are obtainable from avian or reptilian species and one of skill having the knowledge in the art to measure change in absorbance to determine biliverdin would have been able to obtain the same from these species. The samples, whether from human or animal, will be tested the same way because it is the biliverdin compound which is being tested and not the source of the compound. Testing would have been expected to be carried out the same way with the choice of enzyme being the main factor given the type of compound being tested. The Yein et al reference clearly teach that the product species, biliverdin, can be tested as well.

Furthermore, the argument that Falchuk do not teach measuring bilverdin is irrelevant because this is taught by Yein et al as discussed above. Falchuk at least suggests samples comprising biliverdin and further teach reptiles and birds and further teach amphibians do have biliverdin; hence since amphibians and reptiles are cold blooded relatives then there is a suggestion that reptiles will comprise biliverdin. Also birds and reptiles have an evolutionary relationship and birds would have been expected by one of skill in the art to comprise biliverdin. Also, it should be noted that Lin et al teach biliverdin reductase and it would have been obvious to replace the enzyme of Yein et al with the reductase enzyme of Lin et al in order to measure this compound. However, Yein et al also teach that biliverdin can be detected as well as bilrubin, contrary to Applicants' arguments. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that

obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, to measure absorbance to determine biliverdin concentration is clearly suggested by the prior art combination since Yein et al teach the same can be detected and the secondary references teach the other claim features which are not described by Yein et al. To convert biliverdin to bilrubin by adding reductase, as disclosed by Lin et al, and then measure for both compounds using absorbance as dislosed by Yein et al. is clearly an obvious modification of the cited prior art. The claims remain prima facie obvious over the cited prior art and the rejection is sustained.

All claims fail to be patentably distinguishable over the state of the art discussed above and cited on the previously enclosed PTO-892 and/or PTO-1449. Therefore, the claims are properly rejected.

The remaining references listed on the previously enclosed PTO-892 and/or PTO-1449 are cited to further show the state of the art.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah K. Ware whose telephone number is 571-272-0924. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah K. Ware/
Deborah K. Ware
Examiner
Art Unit 1651